Ovarian Cancer 2007 Treatment & Management

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Ovarian Carcinoma--Symptoms

- 95% of women DO report symptoms
  - 80 to 90% of pts with Stage I/ II disease
  - More often, more acute onset of sx, more severe

- Vague and often non-gynecologic
  - abdominal bloating, incr girth, pressure
  - Fatigue
  - GI (nausea, gas, constipation, diarrhea)
  - Urinary frequency/ incontinence
  - Abdominal/ pelvic pain
  - Weight loss/ gain
  - Shortness of breath

Ovarian Cancer: Stage Distribution and Survival

Stage	Percent	5 yr Survival
I--ovary	24	95%
II--pelvis	6	65%
III--abdomen	55	15-30%
IV--distant	15	0-20%
Overall		50%

American Cancer Society 2000

Ovarian Cancer: Risk Factors

Increase	Decrease
Age	Oral Contraceptives (50% decrease)
Family history	Pregnancy and Breastfeeding
Infertility/low parity	
Personal cancer history	Hysterectomy/Removal of Both Ovaries

Ovarian Cancer:
How is Ovarian Cancer Diagnosed?

- Vaginal - rectal exam
- Transvaginal ultrasound
- CA 125 blood test
- Surgical excision/ biopsy

Ovarian Carcinoma
Primary Management

- Initial surgery
  - Thorough surgical staging
  - Aggressive tumor resection (“debulking” cytoreduction)
- Combination chemotherapy

Ovarian Carcinoma
Initial Surgery -- Surgical Staging

- Bilateral Salpingo-oopherectomy / Hysterectomy
- Omentectomy
- Peritoneal biopsies
  - Diaphragm, abdomen, pelvis, small / large bowel mesentery
- Lymphadenectomy
  - Pelvic, para-aortic

Ovarian Carcinoma
Initial Surgery -- Surgical Staging

- Up to 80% of ovarian cancer pts receive inadequate staging from non-gynecologic oncologist

- May translate into choice
  - 2nd surgery to complete staging
  - Chemotherapy for presumed advanced stage

Ovarian Carcinoma
Primary Management—Initial Surgery

- 9 states, 10,432 admissions for ovarian cancer
  - Underwent oopherectomy at minimum
  - Iowa, S Carolina Wisconsin, Florida, Colorado, Maine, New Jersey, New York, Washington

- Comprehensive surgical treatment
  - Lymph node dissection and omentectomy or cytoreduction

  - Diagnosis of secondary malignancy of a specified organ (bowel / peritoneum) with omentectomy / cytoreduction

Goff et al, Cancer 2007

Ovarian Carcinoma
Comprehensive surgical treatment

Hospital / Surgeon characteristics

- 42% received care in teaching hospitals
- 1/3rd pts in low volume hospitals (<10 / yr)
- 25% pts by very-low volume surgeon (1 case/ yr)
- 48% pts by low volume surgeon (<10 cases/ yr)

Goff et al, Cancer 2007

Ovarian Carcinoma
Comprehensive surgical treatment- Hospital

		Rate of Comprehensive Surgery
Annual cases	Low (1-9)	57%
	Medium (10-19)	69%
	High (>20)	74%
Location	Small rural	46%
	Large rural	56%
	Urban	69%

Goff et al, Cancer 2007

Ovarian Carcinoma
Comprehensive surgical treatment- Surgeon

		Rate of Comprehensive Surgery
Annual cases	Very Low (1)	55%
	Medium (2-9)	65%
	High (>10)	75%
Location (Maine only)	Gen Surgeon	38%
	OB/ Gyn	37%
	Gyn Onc	76%

Goff et al, Cancer 2007

Ovarian Carcinoma
Comprehensive surgical treatment- Patient

		OR (95% CI)
Age	21-50	1.00
	51-60	1.07 (0.92-1.26)
	61-70	0.88 (0.74-1.05)
	71-80	0.79 (0.64-0.97)
	>80	0.54 (0.41-0.72)

Goff et al, Cancer 2007

Ovarian Carcinoma
Comprehensive surgical treatment- Patient

		OR (95% CI)
Race	Caucasian	1.00
	African American	0.66 (0.52-0.83)
	Hispanic	0.76 (0.60-0.95)
	Asian/ Islander	0.66 (0.44-0.99)
Stage	Early	1.00
	Advanced	4.78 (4.26-5.37)

Goff et al, Cancer 2007

Ovarian Carcinoma
Primary Management—Debulking

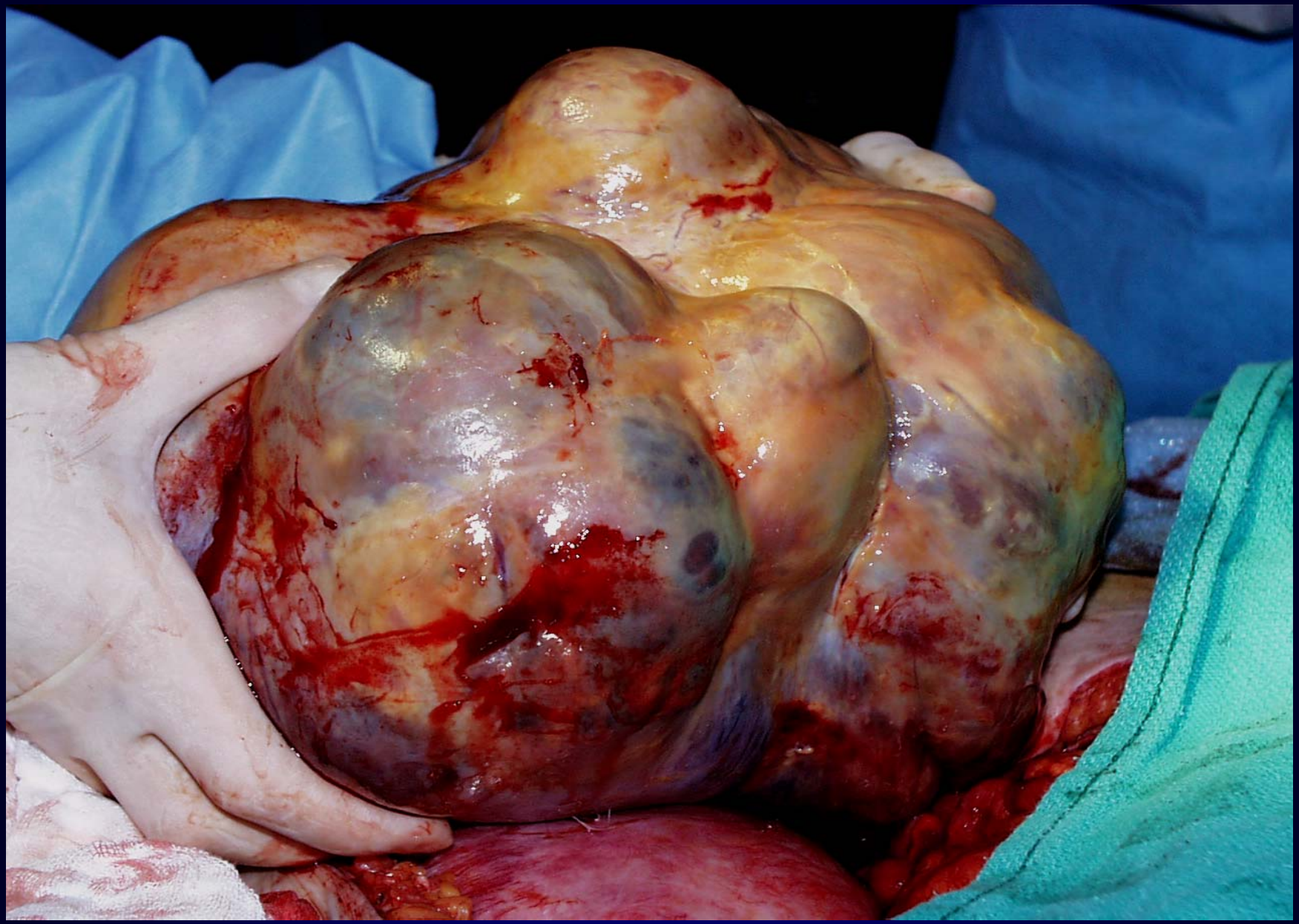
Residual Disease	5 yr survival
< 1 cm	50%
1 to 2 cm	20%
> 2 cm	13%

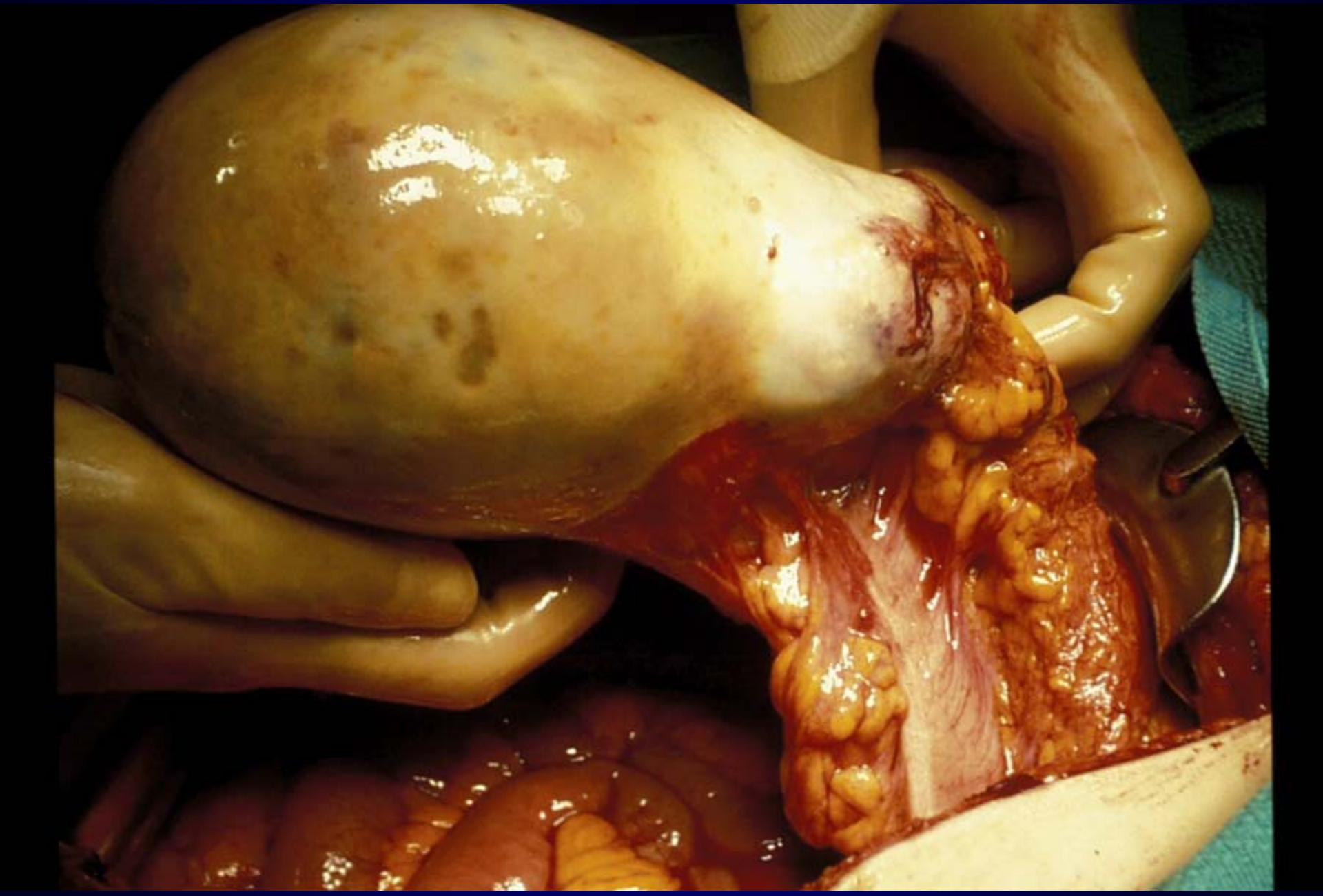
Baker et al, Cancer 1994

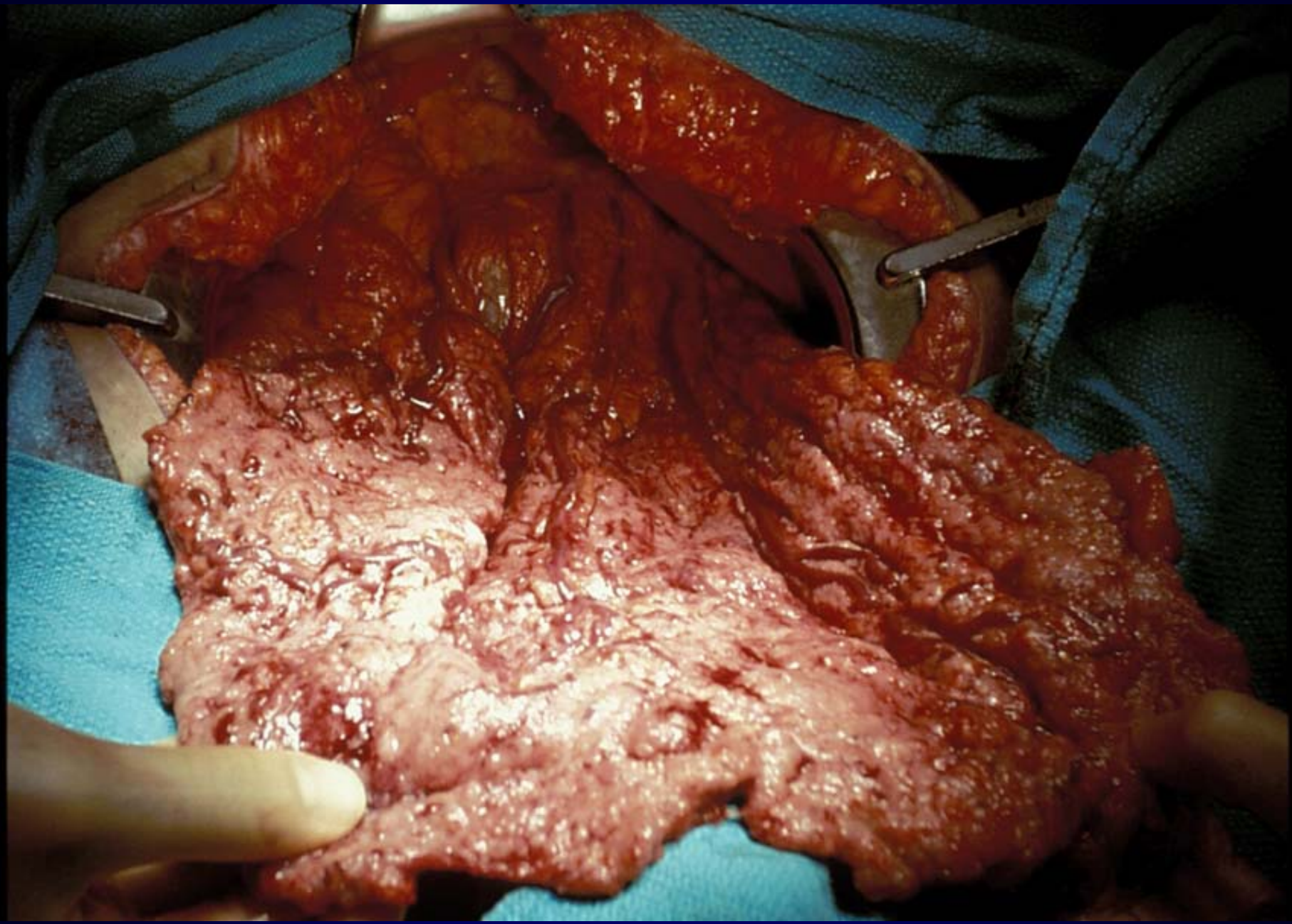
Ovarian Carcinoma
Primary Management—Debulking

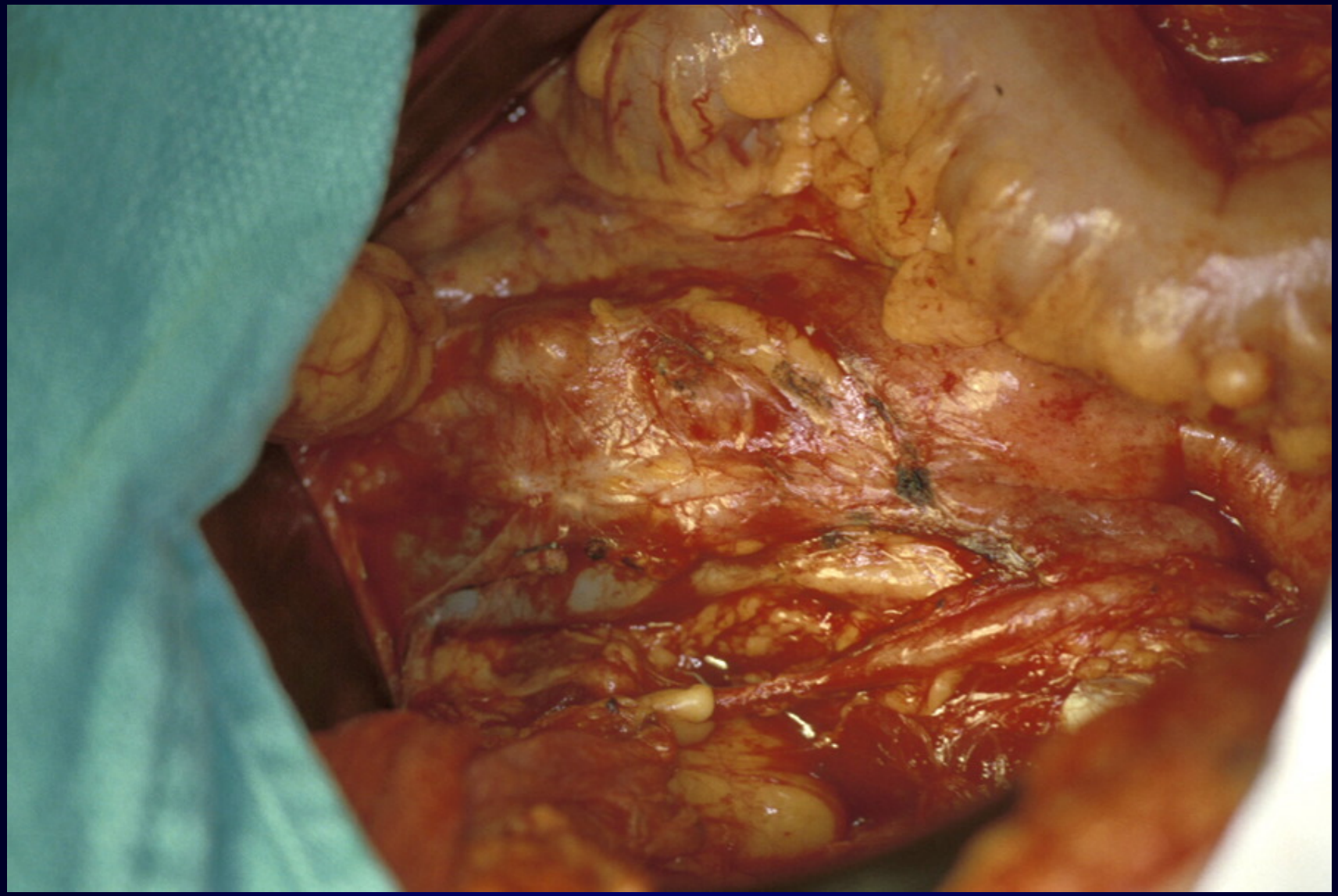
Residual Disease	Median survival
< 0.5cm	40 months
0.5 to 1.5 cm	18 months
> 1.5 cm	6 months

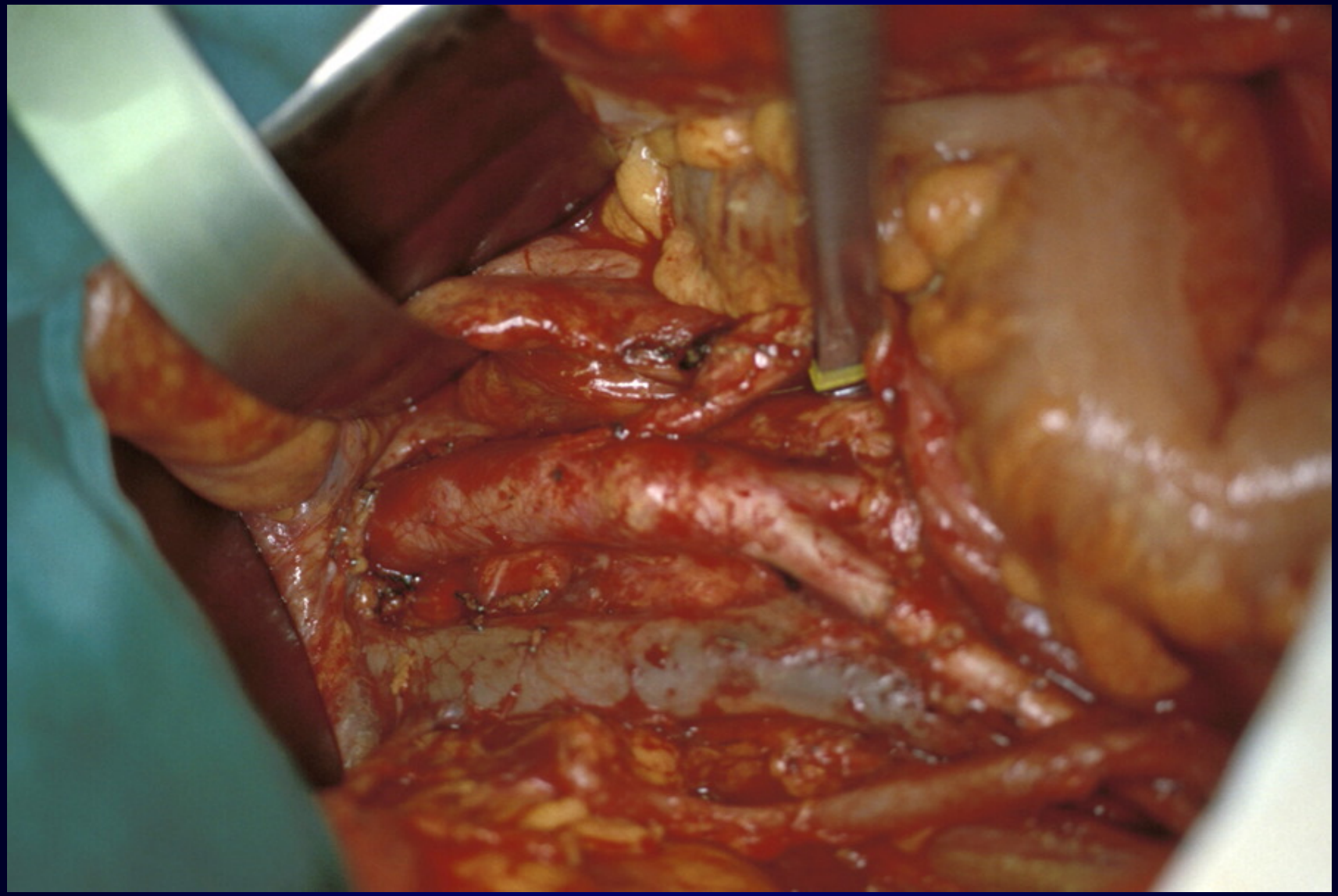
Hacker N, Ob & Gyn 1983











Ovarian Carcinoma
Primary Management—Initial Surgery

- Reoperation within 3 months for debulking/ staging
  - Population based study, 3355 pts
  - Pts less likely to have reoperation if done:
    - In high- or intermed- volume hospital (RR 0.24)
    - By Gyn Onc (RR 0.04 compared to Gen Surgeon)
    - By general Ob/ Gyn (RR 0.37, compared to Gen Surg)
    - By high volume surgeon (RR 0.09)
      (> 10 ovarian cancer cases/ yr)

Elit et al, Gyn Oncol 2002

Ovarian Carcinoma
Primary Management—Initial Surgery

Survival advantage for patients treated by gynecologic oncologist (compared to general OB / Gyn)

- 25% reduction in death at 3yrs (advanced stage)

Junor et al, Br J Ob&Gyn 1999

- 86% vs 70% 5 yr survival Stage I / II
- 21% vs 13% 5 yr survival Stage III / IV

Engelen et al Cancer 2006

Ovarian Cancer in Utah

- Only 39% ovarian Ca patients see a gyn oncologist.
  - 25% of pts > 70 yrs old
  - 27% of pts outside 4 county area
  - 42% of pts in Salt Lake region

Carney et al, Gyn Oncol 2002

Pelvic Mass: Preoperative Prediction of Malignancy

- 5 to 25% premenopausal are malignant
  - 1/3rd in pts < 21 y.o. (solid/ cystic)
  - > 50% in premenarchal pts (solid/ cystic)

- 35 to 63% postmenopausal are malignant
  - Preop assessment of likelihood of malignancy can allow appropriate surgical planning

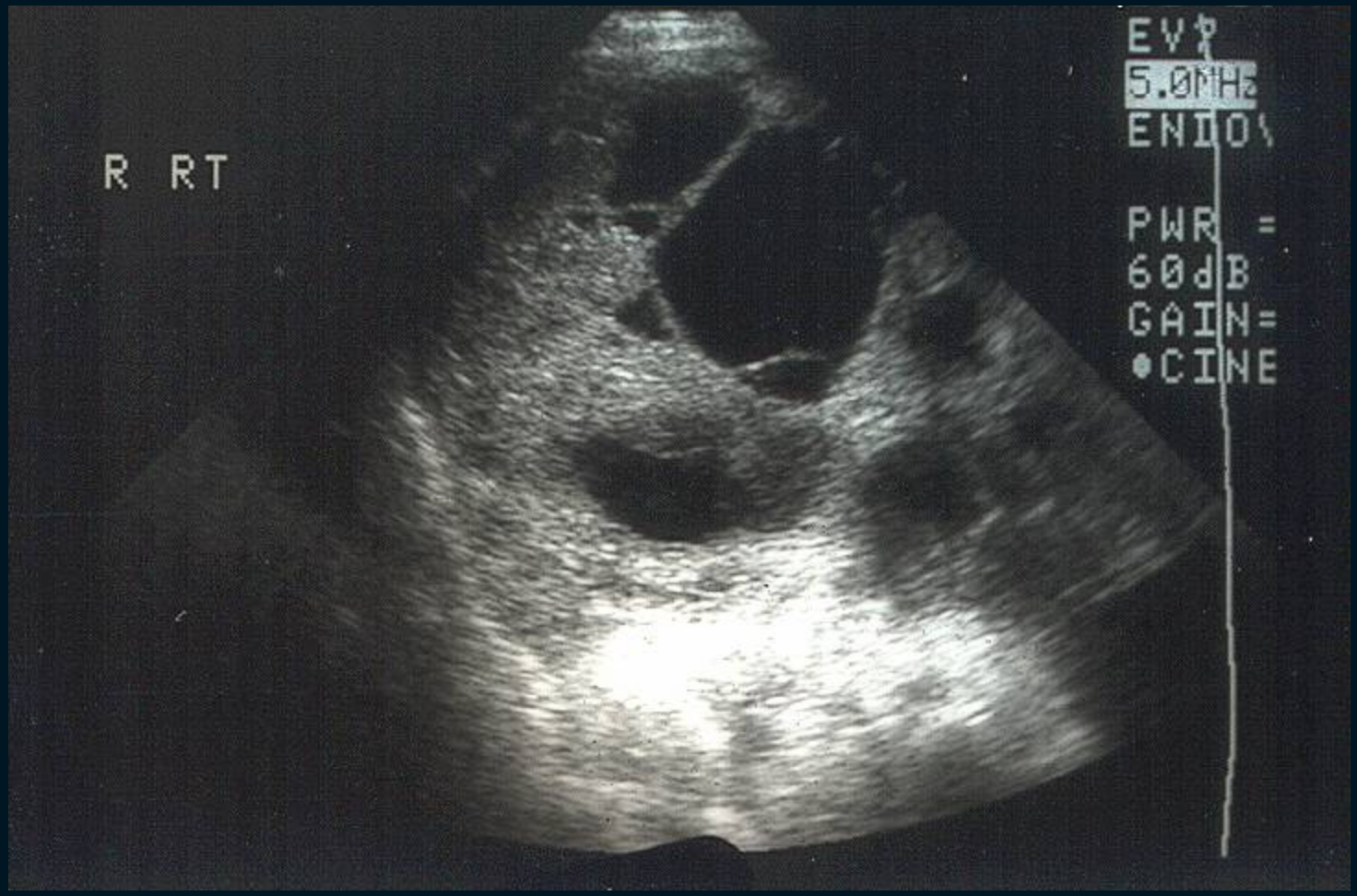
Ovarian Cancer: Hereditary Risks

Family History of Ovarian Cancer	Lifetime Risk
None	1.8%
1 first-degree relative	5%
2 first-degree relatives	7%
Hereditary ovarian cancer syndrome	40%
Known BRCA1 or BRCA2 inherited mutation	20 - 65%

Preoperative Prediction of Malignancy

- Indicators (suspicious)
  - Pelvic examination—fixed, nodular, ascites
  - Tumor markers
    - CA125 > 35U/ mL
    - AFP >10 ng/ mL or hCG >15 mIU/ mL (non pregnant)
    - LDH > 350 U/ L
  - Ultrasonographic findings– solid, cystic with mural nodules

Roman et al, Ob &Gyn 1997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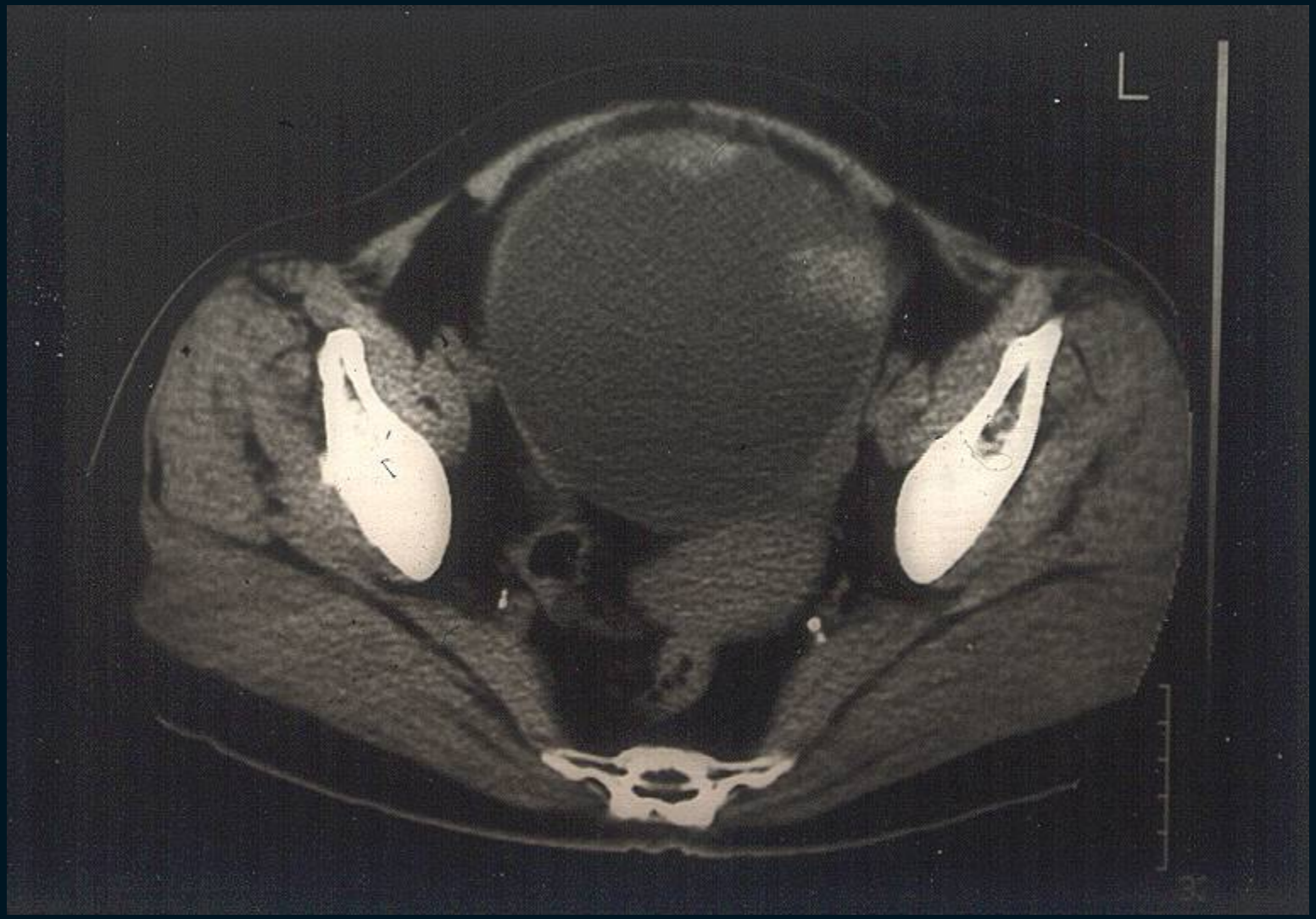
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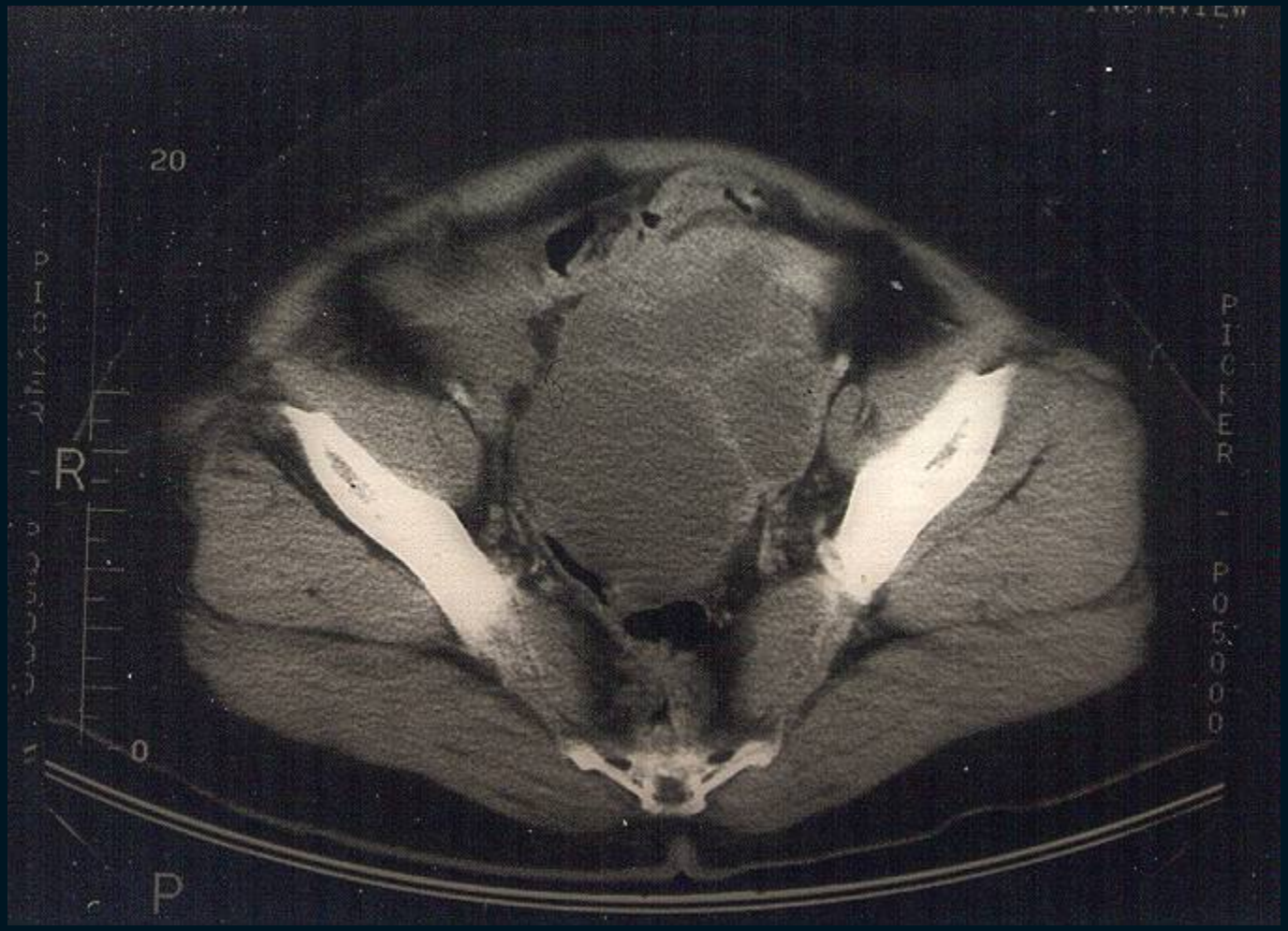
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ACOG / SGO Referral Guidelines Newly Diagnosed Pelvic Mass

- Premenopausal (<50)
  - **CA125 > 200 U/ ml**
  - **ascites**
  - **abd/ distant mets**
  - **Family Hx Breast/ Ovarian cancer (1st degree)**
- Postmenopausal (>50)
  - **CA125 > 35 U/ ml**
  - **ascites**
  - **abd/ distant mets**
  - **Family Hx Breast/ Ovarian cancer (1st degree)**
  - **nodular/ fixed mass**

(Merit referral to gynecologic oncologist)

ACOG Committee Opinion 2002

ACOG / SGO Referral Guidelines Predictive Value

- 1,035 pts, 7 hospitals
- 30% ovarian cancer
- 25% of cancer cases-- premenopausal
- chart / path review
  - CA125
  - preop pelvic exam
  - imaging studies
  - path report

Im et al, Ob &Gyn 2005

Referral Guidelines
Predictive Value--Premenopausal

Criteria	PPV %	NPV %
CA125	70	85
Ascites	58	89
Metastases	64	89
Family Hx	19	82
Overall	34	92

Im et al, Ob &Gyn 2005

Referral Guidelines
Predictive Value--Postmenopausal

Criteria	PPV %	NPV %
CA125	74	85
Ascites	79	72
Pelvic Exam	66	61
Metastases	84	77
Family Hx	42	56
Overall	60	91

Im et al, Ob &Gyn 2005

Referral Guidelines
Patient Distribution

Specialty	Ovarian Cancer	Benign Mass
Premenopausal		
Gyn Onc	70%	31%
OB/ Gyn	30%	69%
Postmenopausal		
Gyn Onc	94%	42%
OB/Gyn	6%	58%

Im et al, Ob &Gyn 2005

Modified Referral Guidelines

- Premenopausal (<50)
  - **CA125 > 50 U/ ml**
  - **ascites**
  - **abd/ distant mets**
- Postmenopausal (>50)
  - **CA125 > 35 U/ ml**
  - **ascites**
  - **abd/ distant mets**

Im et al, Ob &Gyn 2005

Referral Guidelines-- Modified Patient Distribution

Specialty	Ovarian Cancer	Benign Mass
Premenopausal		
Gyn Onc	85%	27%
OB/ Gyn	15%	73%
Postmenopausal		
Gyn Onc	90%	24%
OB/Gyn	10%	76%

Im et al, Ob &Gyn 2005

Ovarian Carcinoma
Primary Management

- Initial surgery
  - Thorough surgical staging
  - Aggressive tumor resection (“debulking”, cytoreduction)

- Combination chemotherapy

Ovarian Cancer
Advances in Chemotherapy

- Gold Standard:
  - Intravenous carboplatin and paclitaxel
  - 6 cycles

- Intraperitoneal Chemotherapy
  - Infused directly into the abdominal cavity
  - Ongoing debate (3 decades!)
  - Recent large, multi-institutional study demonstrated significant, dramatic increase in survival

Ovarian Cancer Intraperitoneal Chemotherapy

- Stage III ovarian/ peritoneal cancer patients
- Randomized, 6 cycles
  - Intravenous paclitaxel & cisplatin

    vs
  - Intravenous paclitaxel & Intraperitoneal cisplatin and paclitaxel
- Progression free survival increased in IP arm
  - 18.3 vs 23.8 months
- Overall survival increased in IP arm
  - 49.7 vs 65.6 months

Armstrong et al, NEJM 2006

Ovarian Cancer Intraperitoneal Chemotherapy

- IP arm had higher and more frequent dosing than IV arm
- Fewer patients in the IP arm were able to complete 6 cycles of the intended therapy
  - 42% completed all 6 IP, rest converted to IV
- IP had higher toxicity rates (heme, GI, neurologic)
- IP had significantly higher survival rates
  - 65 months OS !

Armstrong et al, NEJM 2006

Ovarian Cancer Treatment & Management 2007

- Earlier Diagnosis: ideal
  - symptom recognition
- Initial Surgery: critical
  - Complete staging and cytoreductive surgery
  - Placement of Peritoneal port

Ovarian Cancer Treatment & Management 2007

- Peritoneal Chemotherapy: significant advance
- Integrated Care
  - Patients
  - Primary providers
  - Gynecologic Oncologists
  - Medical Oncologists

References

Armstrong et al, NEJM 2006; NEJM, 354:34-43

American College of Obstetricians & Gynecologists, Committee Opinion 2002

Baker et al, Cancer 1994;74:656-63

Carney et al, Gynecologic Oncology 2002;99:888-91

Elit et al, Gynecologic Oncology 2002;87:260-7

Engelen et al, Cancer 2006;106:589-98

Goff et al, Cancer 2007;109:2031-42

Hacker et al, Obstetrics & Gynecology 1983;61:408-12

Im et al, Obstetrics & Gynecology 2005

Junor et al, British J Obstetrics & Gynecology 1999;106:1130-6

Roman et al, Obstetrics & Gynecology 1997;89:493-500